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EXAMINER	
KAPUSHOC, STEPHEN THOMAS	
ART UNIT	**PAPER NUMBER**
1634	

DATE MAILED: 10/10/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/824,656	FRANZEN ET AL.	
	Examiner	Art Unit	
	Stephen Kapushoc	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-19* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-19* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *14 April 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *11/26; 3/10; 8/18*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-19 are pending and examined on the merits.

Information Disclosure Statement

The IDS of 11/26/2004, 3/10/2006, and 8/18/2006 have been considered. The reference cited on 8/18/2006 has been lined through, as it is a duplicate of a reference provided on the IDS of 3/10/2006.

Claim Rejections - 35 USC § 112

1. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

2. Claims 1-19 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1-19 are unclear over the stated purpose of the claimed method of 'measuring the binding of analyte molecules to probe molecules' as recited in claim 1. The final process step of claim 1 recites 'detecting the binding of the analyte molecules'. It is thus unclear how the detecting the binding of analyte molecules relates to measuring the binding of analyte molecules, as the act of detecting (e.g. a qualitative measurement) is not synonymous with measuring, which requires a quantitavtive component.

Claims 1-19 are unclear over recitation of the phrase 'and, together with the analyte molecules, electrically conductive nanoparticles' in step (c) of claims 1. It is unclear if applicant intends, for example, for the nanoparticles to participate in the binding of the analyte molecule to the probe molecules, or for the nanoparticles to interact directly with the probe molecules.

Claims 1-19 are unclear over recitation of the phrase 'making the circuits of the circuit surface electrically reading the presence of the nanoparticles' in step (d) of claim 1, as it is unclear what is intended by or required for 'making the circuits of the circuit surface electrically', and if such a process is 'reading the presence of the nanoparticles', or a separate step is required for reading the presence of the nanoparticle.

Claim 2 is unclear over recitation of the phrase 'the circuit', because there is no antecedent basis for any particular circuit in the claim. Claim 1 recites only a 'surface with electronic circuits', thus it is unclear if applicant intends 'the circuit' of claim 2 to be a specific circuit.

Claims 3, 9, and 13-17 are unclear over recitation of the phrase 'the circuit' in claims 3, because there is no antecedent basis for any particular circuit in the claim. Claim 1 recites only a 'surface with electronic circuits', thus it is unclear if applicant intends 'the circuit' of claim 3 to be a specific circuit.

Claims 3 and 9-17 are unclear over recitation of the phrase 'reading a voltage on the nanoparticles' as it is unclear if, for example, the nanoparticles themselves provide a measurement of voltage, or a voltage is conducted by the nanoparticles.

Claim 7 is unclear over recitation of the phrase 'the nanoparticles are already bound to the analyte molecules' because claim 1,from which the rejected claims depend, recites several steps and it is thus unclear if applicant intends the term 'already' to indicate that the nanoparticles are bound prior to any particular step.

Claims 9 and 13-17 are unclear over recitation of the phrase 'the countersurface' in claim 9, as there is no antecedent basis in the claims for any countersurface.

Claims 9 and 13-17 are unclear over recitation of the phrase 'measured via the nanoparticles in the circuits', as it is unclear if the nanoparticles are themselves somehow measuring a voltage.

Claims 10-12 are unclear over recitation of the phrase 'the metal surface' in claim 10, as there is no antecedent basis in the claims for any metal surface.

Claim 15 is unclear as the claim recites limitations that indicate that contact between the nanoparticles and a contact spot is made 'by an external magnetic field', however the claim is dependent from claim 9 which recites the limitation that 'the nanoparticles are pressed against a contact spot of the circuit by a movement of the countersurface'. It is thus unclear is the claim requires contact to be made by a magnetic field or movement of a countersurface.

Claims 18 and 19 are unclear over recitation of the phrase 'amplified in a previous step' because claim 1, from which the rejected claims depend, recites several steps and it is thus unclear if applicant intends the term 'already' to indicate that the nanoparticles are bound prior to any particular step.

Claims 18 and 19 are unclear over recitation of the phrase 'the biotin groups of the analyte molecules' because there is no antecedent basis in the claims for any biotin groups of the analyte molecules.

Claims 18 and 19 are unclear over recitation of the phrase 'by being coated with streptavidin' because it is what is intended by the phrase.

Claim 19 is unclear over recitation of the phrase 'the biotin-streptavidin binding pair' as there is not proper antecedent basis for a particular biding pair in the claim. It is additionally unclear if the claim, which is dependent upon claim 18, requires the use of a biotinylated primer and streptavidin coated nanoparticles, as required by claim 18, or if the substitution with 'another binding pair' requires different elements than those recited in the base claim.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

3. Claims 1-4, 6, 7, 8, 10, 11, 18 and 19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Knoll (1999; WO 99/27367) in view of Henkens et al (2002, US Patent 6,391,558).

This rejection is made using the publication date of PCT/EP98/07494. The publication is in German, thus the Examiner has relied upon the English translation

provide by US Patent 6,548,311, which is a 371 from the aforementioned International application. Cited portions of the reference in this rejection are based upon the US Patent 6,548,311 publication column and line numbers.

Regarding claim 1, Knoll teaches providing a circuit surface with electronic circuits (see for example Fig 11 and 14), relevant to step (a), and providing immobilized probe molecules in spatial proximity to the circuits (see for example Fig 9 and 10). The reference further teaches the binding of analyte molecules to the immobilized probe molecules and the further binding of electrically conductive nanoparticles (termed in the reference 'marker particles' (col.13 ln.66 – col.14 ln.9) (for example col.11 lns.10-12), relevant to step (c). Relevant to step (d), Knoll teaches the detection of the marker particles using an electrical circuit (for example col.13 lns.12-24; Fig 17).

Regarding claim 2, Knoll teaches that the detection involves measuring changes in capacity between electrodes (for example col.4 lns.4-7; col.8 lns.25-30).

Regarding claim 3, Knoll teaches that the nanoparticles contact a contact spot (for example Fig 10 indicates that the marker particle attached to a reporter probe contacts the electrode by hybridization of the reporter probe to the analyte at the electrode (for example Fig 10 and Figs 1, 3), and further teaches detection by measuring voltage (col.8 lns.25-30).

Regarding claim 4, Knoll teaches probe molecules bound to the circuit surface (for example Fig 10).

Regarding claim 6, Knoll teaches probe molecules immobilized to an electrode surface, and analyte molecules affinity bound (e.g. antibody-antigen, Fig 5; DNA:DNA / probe:analyte hybridization) to the probe molecules.

Regarding claims 7 and 8, Knoll teaches the marker particle bound to the analyte prior to hybridization (Fig 9), thus already bound to the analyte molecule, relevant to claim 7, and nanoparticles with adhesion molecules (e.g. the reporter probe of Knoll is an adhesion molecule) attached to analyte molecules bound to surface bound probes (Fig 10) relevant to claim 8.

Regarding claim 10 and 11, Knoll teaches the detection of analytes using potentiometric measurement methods (col.18 ln.30 – col.20 ln.5) where contact of an electroconductive marker to a potentiometric electrode allows ions to flow through an aqueous measuring medium (which is thus an electrolyte) to generate an electric current. Relevant to claim 11, Knoll teaches that the marker particles may be conductive (col.14 lns.5-9), thus they are electrically conductive molecules.

Knoll does not particularly state that the immobilized probe (part 13 in Fig 10) is bound to the circuit surface by a covalent bond, or provide any particular details regarding the binding of the marker particle (part 5 in Fig 9) to the analyte molecule (parts 11 and 11' in Fig 9).

Henkens et al teaches methods for the detection of nucleic acids using electrodes comprising immobilized probes, as well as analyte molecules labeled with detectable reporters. Henkens et al specifically teaches that capture probes may be covalently bound to an electrode (col.45 lns.16-25).

Regarding claims 18 and 19, Henkens et al teaches the PCR amplification of a analyte DNA molecule using primers modified at the 5' end, and gives the examples of fluorescein and biotin labeled primers (col.21 ln.60 - col 22. ln.4). Henkens et al indicates that the resulting labeled PCR product may be attached to a reporter molecule by an interaction between the label from the PCR primer and a binding partner for the label of the primer. Relevant to claim 19, Henkens et al particularly teaches biding of a fluorescein-labeled PCR product to an anti-fluorescein HRP conjugate. Relevant to claim 18, Henkens et al teaches the biotin:avidin binding pair, as well as labeling a PCR product using a biotinylated primer, and binding of the labeled PCR product to a avidin-gold biding partner (for example col.5 lns.25-35, col.43 ln.55).

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have used the nucleic acid probe immobilization methods of Henkens et al in the electrode based analysis methods of Knoll. One would have been motivated to do so based on the assertion of Henkens et al that covalent attachment of a probe is a preferred method (col.45 lns. 16-25). It would further have been obvious to use the probe:reporter binding method of Henkens et al to accomplish the marker particle:analyte binding of Knoll et al. One would have been motivated to do so because Henkens et al teaches that such methods can be used to attach a variety of different molecules (including colloidal gold which is similar to the description of marker particles by Knoll) to nucleic acid for analysis.

4. Claims 5 and 12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Knoll (1999; WO 99/27367) in view of Henkens et al (2002, US Patent 6,391,558) and further in view of Wohlstadter et al (2001, US Patent 6,207,369).

The teachings of Knoll in view of Henkens et al are applied to claims 5 and 12 as they were previously applied to claims 1-4, 6, 7, 8, 10, 11, 18 and 19.

Knoll in view of Henkens et al does not specifically teach probe molecules bound to a countersurface positioned opposite the circuit surface (claim 5), or the use of polyene molecules to conduct an electrical signal (claim 12).

Regarding claim 5, Wohlstadter et al teaches methods of using several configurations of electrode-based devices in which the portion of the device where the analyte is collected (termed in the reference the 'binding domain') is on a surface opposite from an electrode (see for example Fig. 21 and Fig. 37).

Regarding claim 12, Wohlstadter et al teaches the use of a linking chain to ensure low resistance of electron transfer from the electrode, and specifically teaches the use of a polyacetylene chain (col.39 lns.53-63), which is on the polyene class.

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have performed the electronic detection methods of Knoll in view of Henkens et al using a probe binding area on a countersurface opposing an electrode. One would have been motivated to do so based on the teachings of Wohlstadter et al that in such a configuration the electrode can be protected during the binding reaction from the sample by a physical barrier that is subsequently removed thus, preventing contamination of the electrode surface which could result in a change

in its electrochemical performance (col.64 lns.1-11). One would have a reasonable expectation of success because Wohlstadter et al teaches that the binding domain of the countersurface makes contact with the electrode and carries current from the counter electrode to the working electrode (col.45 lns.9-35). It would have been further obvious to use the polyacetlyene chains of Wohlstadter et al to ensure low resistance of conductivity from the electrode to the marker particle as Wohlstadter et al teaches this use for polyacetylene chains.

5. Claims 9, 13, 16, and 17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Knoll (1999; WO 99/27367) in view of Henkens et al (2002, US Patent 6,391,558) and further in view of Fish (2002, WO 02/054052 A1).

The teachings of Knoll in view of Henkens et al are applied to claims 5 and 12 as they were previously applied to claims 1-4, 6, 7, 8, 10, 11, 18 and 19.

Relevant to claim 16, Knoll specifically teaches that the marker particles may be magnetic (see for example col.4 lns.10-24).

Relevant to claim 17, Knoll teaches that the marker particles my be dendrimers (col.14 lns.2-3), which are protrusions.

Knoll in view of Henkens et al does not teach the movement of a countersurface to press nanoparticles against a contact spot.

Regarding claim 9, Fish teaches the detection of analytes using an electrode-based method wherein an opposing surface with an electrode is moved to make contact

with an electrically readable particle that is bound to analyte, where the analyte is bound to an immobilized probe (see for example Fig 1, p.14-18).

Regarding claim 13, Fish specifically teaches that pressure is applied to the particle (p.16 last two lines) and that the bound particles make contact with the electrode (p.17 lns.7-8).

Regarding claim 16, Fish teaches that a countersurface may be moved in order to create a physical contact between an electrode (which is a contact spot) and an electrically readable particle, and also teaches that the probes may be attached to a contact spot and that movement of the countersurface causes the particles to make contact with the contact spot (see for example Fig 13 and page 28).

Additionally relevant to claim 17, Fish teaches that an electrode may be rough and have sharp edges and vertices to make electrical contact (p.42), thus teaching a circuit surface with electrically conductive protrusions.

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have performed the electrode-based analyte detection method of Knoll in view of Henkens et al by incorporating the countersurface movement taught by Fish to make contact between a particle and an electrode. One would have been motivated to do so based on the teachings of Fish that such methods allow accurate electrochemistry to be performed quickly at a low cost (p.7). One would have had a reasonable expectation of success because Knoll teaches that the electrode-based method can be used as a multi-step process separating the steps of particle transport and electrode binding (col. 5 lns.62-67).

6. Claim 14 is rejected under 35 U.S.C. 103(a) as being unpatentable over Knoll (1999; WO 99/27367) in view of Henkens et al (2002, US Patent 6,391,558) and Fish (2002, WO 02/054052 A1), and further in view of Wohlstadter et al (2001, US Patent 6,207,369).

The teachings of Knoll in view of Henkens et al and Fish are applied to claim 14 as they were previously applied to claims 9, 13, 16, and 17.

Knoll in view of Henkens et al and Fish teaches an electrode-based method of analyte detection wherein marker particles bind to analyte molecules and contact between the marker particle and a contact spot is made the movement of surfaces to press the particle to the contact spot.

Knoll in view of Henkens et al and Fish does not specifically teach that the analyte molecule:particle complex is located on a surface opposite the circuit surface.

Wohlstadter et al teaches methods of using several configurations of electrode-based devices in which the portion of the device where the analyte is collected (termed in the reference the 'binding domain') is on a surface opposite from an electrode (see for example Fig. 21 and Fig. 37).

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have used the opposed binding and electrode surfaces taught by Wohlstader et al in the electrode-based analyte detection method of Knoll in view of Henkens et al and Fish. One would have been motivated to do so based on the teachings of Wohlstadter et al that in such a configuration the electrode can be

protected during the binding reaction from the sample by a physical barrier that is subsequently removed thus, preventing contamination of the electrode surface which could result in a change in its electrochemical performance (col.64 lns.1-11).

7. Claim 15 is rejected under 35 U.S.C. 103(a) as being unpatentable over Knoll (1999; WO 99/27367) in view of Henkens et al (2002, US Patent 6,391,558), Fish (2002, WO 02/054052 A1), and Wohlstadter et al (2001, US Patent 6,207,369) and Wang et al (2001).

The teachings of Knoll in view of Henkens et al and Fish are applied to claim 15 as they were previously applied to claims 9, 13, 16, and 17.

Knoll in view of Henkens et al and Fish teaches an electrode-based method of analyte detection wherein marker particles bind to analyte molecules and contact between the marker particle and a contact spot is made the movement of surfaces to press the particle to the contact spot, as required by claims 9 and 13 from which the rejected claim 15 depends. Further relevant to claim 15, Knoll teaches that marker particles may be magnetic (see for example col.4 lns.10-24) and moved by a magnetic field (col.9 lns.22-25; Figs 16, 20 and 21), and that marker particles may be coated with metal (col14, lns.4-9).

Knoll in view of Henkens et al and Fish does not specifically teach that the analyte molecule:particle complex is located on a surface opposite the circuit surface, or that the linkage between the particle and the analyte molecule is broken.

Wohlstadter et al teaches methods of using several configurations of electrode-based devices in which the portion of the device where the analyte is collected (termed in the reference the 'binding domain') is on a surface opposite from an electrode (see for example Fig. 21 and Fig. 37).

Wang et al teaches an electrode-based method for the detection of an analyte (e.g. the detection of DNA hybridization). The reference teaches a method in which a gold nanoparticle binds to a target oligonucleotide wherein the target oligonucleotide has hybridized to a probe oligonucleotide immobilized to a solid support (Fig 1; p.5577, left col., lns.5-10). The method of Wang et al includes a step of dissolution of the gold nanoparticle from the analyte molecule prior to detection of the gold nanoparticle at an electrode.

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have incorporated the used the opposed binding and electrode surfaces taught by Wohlstader et al in the electrode-based analyte detection method of Knoll in view of Henkens et al and Fish. One would have been motivated to do so based on the teachings of Wohlstadter et al that in such a configuration the electrode can be protected during the binding reaction from the sample by a physical barrier that is subsequently removed thus, preventing contamination of the electrode surface which could result in a change in its electrochemical performance (col.64 lns.1-11). It would have been further obvious to use the dissolution of a gold microparticle from a bound analyte molecule as taught by Wang et al as a detectable nanoparticle. One would have bee motivated to use such a method because Wang et al teaches the

sensitivity ((p.5581, left col., lns.13-16) and adaptability (p.5581, right col., lns.17-19) of such a technique. Incorporating the methods of Wang et al into the teachings of Knoll et al would result in the use of a magnetic field to move an electrically conductive and magnetic marker particle to an electrode after separation of the particle from a particle:analyte:probe complex.

Conclusion

8. No claim is allowable. No claim is free of the prior art.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stephen Kapushoc whose telephone number is 571-272-3312. The examiner can normally be reached on Monday through Friday, from 8am until 5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached at 571-272-0735. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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PRIMARY EXAMINER